Guidance for Industry

Formal Meetings Between the FDA and Biosimilar Biological Product Sponsors or Applicants

DRAFT GUIDANCE

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For questions regarding this draft document contact (CDER) Neel Patel at 301-796-0970 or (CBER) the Office of Communication, Outreach, and Development at 800-835-4709 or 301-827-1800.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

March 2013
Procedural

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This draft guidance, when finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

I. INTRODUCTION

This guidance provides recommendations to industry on formal meetings between the Food and Drug Administration (FDA) and biosimilar biological product sponsors or applicants. The Biosimilar User Fee Act of 2012 (BsUFA), enacted as part of the Food and Drug Administration Safety and Innovation Act (FDASIA), amended the Federal Food, Drug, and Cosmetic Act (FD&C Act) to authorize a new user fee program for biosimilar biological products.[2,3] The FDA has committed to meeting certain performance goals set forth in a letter from the Secretary of Health and Human Services to the Chairman of the Committee on Health, Education, Labor, and Pensions of the Senate and the Chairman of the Committee on Energy and Commerce of the House of Representatives.[4] The performance goals include meeting management goals for formal meetings that occur between the FDA and sponsors or applicants during the development phase of a biosimilar biological product. The FDA encourages sponsors and applicants to use

[1] This guidance has been prepared by the Center for Drug Evaluation and Research (CDER) in cooperation with the Center for Biologics Evaluation and Research (CBER) at the Food and Drug Administration.

[2] For the statutory definition of *biosimilar* and *biological product* and definitions of selected terms used in this guidance, see the terminology section of the draft guidance for industry *Scientific Considerations in Demonstrating Biosimilarity to a Reference Product*. (When final, this guidance will represent the FDA's current thinking on this topic. For the most recent version of a guidance, check the FDA Drugs guidance Web page at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.) For the statutory definition of *biosimilar biological product application*, see section 744G(4) of the FD&C Act.

[3] Sections 401-408 of FDASIA, adding sections 744G, 744H, and 744I to the FD&C Act.

[4] The BsUFA goals letter, which is titled "Biosimilar Biological Product Authorization Performance Goals and Procedures Fiscal Years 2013 Through 3 2017," is available on the FDA's Web site at http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/Biosimilars/UCM281991.pdf.

the meetings described in this guidance to optimize product development and facilitate submission of marketing applications.

For the purposes of this guidance, *formal meeting* includes any meeting that is requested by a sponsor or applicant following the request procedures provided in this guidance and includes meetings conducted in any format (i.e., face-to-face meeting, teleconference, or videoconference).

This guidance reflects a unified approach to all formal meetings between sponsors or applicants and the FDA for biosimilar biological product development (BPD) programs. This guidance is intended to assist sponsors or applicants in generating and submitting a meeting request and the associated meeting package to the FDA for biosimilar biological products intended to be submitted under 351(k) of the Public Health Service Act (PHS Act). This guidance does not apply to meetings associated with new drug applications or abbreviated new drug applications under section 505 of the FD&C Act or to biologics license applications (BLAs) under section 351(a) of the PHS Act.[5]

This guidance discusses the principles of good meeting management practices (GMMPs) and describes standardized procedures for requesting, preparing, scheduling, conducting, and documenting such formal meetings.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. BACKGROUND

The FDA expects review staff to participate in many meetings with biosimilar biological product sponsors or applicants who seek guidance relating to the development and review of biosimilar biological products. Because these meetings often will represent critical points in the regulatory and development process, it is important that there are efficient, consistent procedures for the timely and effective conduct of such meetings. The GMMPs in this guidance are intended to provide consistent procedures that will promote well-managed meetings, and ensure that such meetings are scheduled within a reasonable time, conducted efficiently, and documented appropriately.

[5] For information on meetings for new drug applications and 351(a) BLAs, see the guidance for industry *Formal Meetings Between the FDA and Sponsors or Applicants*. We update guidances periodically. To make sure you have the most recent version of a guidance, check the FDA Drugs guidance Web page at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.

III. MEETINGS TYPES[6]

There are five types of formal meetings that can occur between sponsors or applicants and FDA staff to discuss development of a biosimilar biological product:

1. **Biosimilar Initial Advisory meeting:** A Biosimilar Initial Advisory meeting is an initial assessment limited to a general discussion regarding whether licensure under section 351(k) of the PHS Act may be feasible for a particular product, and, if so, general advice on the expected content of the development program. This meeting type does not include any meeting that involves substantive review of summary data or full study reports. However, preliminary comparative analytical similarity data should be provided with the meeting request to enable the FDA to make a preliminary determination as to whether licensure under section 351(k) of the PHS Act may be feasible for a particular product, and to provide meaningful advice. An overview of the proposed development program also should be provided.

2. **BPD Type 1 meeting:** A BPD Type 1 meeting is a meeting that is necessary for an otherwise stalled BPD program to proceed. Examples of a BPD Type 1 meeting include:

   - Meetings to discuss clinical holds in which a response to hold issues has been submitted, but the FDA and the sponsor or applicant agree that the development is stalled and a new path forward should be discussed

   - Special protocol assessment meetings that are requested by sponsors or applicants after receipt of FDA evaluation of protocols under the special protocol assessment procedures as described in Section VI of the BsUFA goals letter

   - Meetings to discuss an important safety issue, when such an issue is identified and the FDA and the sponsor or applicant agree that the issue should be discussed

   - Dispute resolution meetings as described in 21 CFR 10.75 and 312.48, and in Section IV of the BsUFA goals letter, and the draft guidance for industry and review staff *Formal Dispute Resolution: Appeals Above the Division Level*[7]

3. **BPD Type 2 meeting:** A BPD Type 2 meeting is a meeting to discuss a specific issue (e.g., proposed study design or endpoints) or questions where the FDA will provide targeted advice regarding an ongoing BPD program. This meeting type includes substantive review of summary data, but does not include review of full study reports.

[6] The meeting types and goal dates for BPD meetings were developed by the FDA in consultation with public and industry stakeholders as directed by the Biologics Price Competition and Innovation Act of 2009 (BPCI Act). For more information about BsUFA and the fee criteria for BPD meetings, refer to the BsUFA Web page at http://www.fda.gov/ForIndustry/UserFees/BiosimilarUserFeeActBsUFA/default.htm.

[7] When final, this guidance will represent the FDA's current thinking on this topic.

4. **BPD Type 3 meeting:** A BPD Type 3 meeting is an in-depth data review and advice meeting regarding an ongoing BPD program. This meeting type includes substantive review of full study reports, FDA advice regarding the similarity between the proposed biosimilar biological product and the reference product, and FDA advice regarding the need for additional studies, including design and analysis.

5. **BPD Type 4 meeting:** A BPD Type 4 meeting is a meeting to discuss the format and content of a biosimilar biological product application or supplement to be submitted under section 351(k) of the PHS Act.

IV. PARTICIPATION IN THE FDA'S BIOSIMILAR BIOLOGICAL PRODUCT DEVELOPMENT PROGRAM

As stipulated by statute, a sponsor or applicant must pay a biosimilar biological product development fee (BPD fee) to participate in the FDA's BPD program to receive a BPD Type 1, 2, 3, or 4 meeting for a product.[8] There is no fee for a Biosimilar Initial Advisory meeting. The BPD fee is an annual per-product fee, not a per-meeting or per-review activity fee. There are three types of BPD fees: the initial BPD fee, the annual BPD fee, and the reactivation fee. The initial BPD fee is due on the date a sponsor or applicant submits an investigational new drug application (IND) for an investigation that the FDA determines is intended to support a biosimilar biological product application for a product, or within 5 calendar days after the FDA grants the sponsor's or applicant's request for a BPD Type 1, 2, 3, or 4 meeting for that product, whichever occurs first.[9]

After a sponsor or applicant has paid the initial BPD fee, beginning in the next fiscal year, an annual BPD fee will be assessed for the product until the sponsor or applicant submits a marketing application that is accepted for filing, or discontinues participation in the BPD program for that product.[10] If a sponsor or applicant has discontinued participation in the BPD program for a product and wants to again engage with the FDA on development of the product as a biosimilar biological product, the sponsor must pay a reactivation fee to resume participation in the BPD program for that product.[11] The reactivation fee is due on the date the sponsor submits an IND for an investigation that the FDA determines is intended to support a biosimilar biological product application for the product, or within 5 calendar days after the FDA grants the sponsor's or applicant's request for a BPD Type 1, 2, 3, or 4 meeting for the product, whichever occurs first.[12]

[8] See section 744H(a)(1)(E) of the FD&C Act.

[9] See section 744H(a)(1)(A) of the FD&C Act.

[10] See section 744H(a)(1)(B) of the FD&C Act.

[11] See section 744H(a)(1)(D) of the FD&C Act.

[12] Id.

Section 744H(a)(1)(E) of the FD&C Act establishes the consequences of failure to pay BPD fees. With respect to meetings, if the FDA grants a request for a BPD Type 1, 2, 3, or 4 meeting for a product, and the granting of the meeting request triggers an obligation to pay an initial BPD fee or a reactivation fee for the product, the meeting will be cancelled if the sponsor or applicant fails to pay the fee within 5 calendar days after the meeting is officially granted.[13] Additionally, if a sponsor or applicant is in arrears with respect to an annual BPD fee for a product, the FDA will deny the sponsor's or applicant's request for a BPD Type 1, 2, 3, or 4 meeting for that product, and cancel any scheduled BPD meetings for that product.[14]

V. MEETING PROCEDURES

Each meeting type is subject to different procedures, as described below.

A. Biosimilar Initial Advisory Meeting

Biosimilar Initial Advisory meetings should be scheduled to occur within 90 calendar days of FDA receipt of a written meeting request and meeting package. If a sponsor or applicant requests a meeting date that is beyond 90 days from the date of the request receipt, the FDA will work with the sponsor or applicant to determine the earliest agreeable date.

B. BPD Type 1 Meeting

If sponsors or applicants are considering submission of a request for a BPD Type 1 meeting, they should first contact the relevant division in either the Center for Biologics Evaluation and Research (CBER) or the Center for Drug Evaluation and Research (CDER) to discuss the suitability of the request. BPD Type 1 meetings should be scheduled to occur within 30 calendar days of FDA receipt of a written meeting request and meeting package. If a sponsor or applicant requests a meeting date that is beyond 30 days from the date of the request receipt, the FDA will work with the sponsor or applicant to determine the earliest agreeable date.

C. BPD Type 2 Meeting

BPD Type 2 meetings should be scheduled to occur within 75 calendar days of FDA receipt of a written meeting request and meeting package. If a sponsor or applicant requests a meeting date that is beyond 75 days from the date of request receipt, the FDA will work with the sponsor or applicant to determine the earliest agreeable date.

D. BPD Type 3 Meeting

BPD Type 3 meetings should be scheduled to occur within 120 calendar days of FDA receipt of a written meeting request and meeting package. If a sponsor or applicant requests a meeting date

[13] See section 744H(a)(1)(E) of the FD&C Act.

[14] Id.

that is beyond 120 days from the date of the request receipt, the FDA will work with the sponsor or applicant to determine the earliest agreeable date.

E. BPD Type 4 Meeting

BPD Type 4 meetings should be scheduled to occur within 60 calendar days of FDA receipt of a written meeting request and meeting package. If a sponsor or applicant requests a meeting date that is beyond 60 days from the date of the request receipt, the FDA will work with the sponsor or applicant to determine the earliest agreeable date.

VI. MEETING REQUESTS BY SPONSORS OR APPLICANTS

To make the most efficient use of FDA resources, before seeking a meeting with CBER or CDER, sponsors or applicants should consider other sources of information applicable to their product development program, such as FDA and International Conference on Harmonisation guidances. Written correspondence to request such a meeting should be submitted to the sponsor's or applicant's application (e.g., IND, BLA) through the controlled document system.[15]

If there is no application, the request should be submitted to either the appropriate CDER division director with a copy sent to the division's chief of project management staff or to the division director of the appropriate product office within CBER. Before submitting any meeting request by fax or email when there is no application, the sponsor or applicant should contact the appropriate product office within CBER, or the appropriate division or the Biosimilars Program staff within CDER, Office of New Drugs, to determine to whom the request should be directed, how the request should be submitted, and the appropriate format for the request, and to arrange for confirmation of receipt of the request. This contact reduces the possibility that faxed or emailed requests will be inadvertently overlooked because of the volume of emails and faxes received daily by FDA staff. Faxed or emailed requests should be sent during official business hours (8:00 a.m. to 4:30 p.m. EST/EDT) Monday through Friday (except Federal government holidays). Processing and receipt may be delayed for requests where confirmation of receipt has not been prearranged.

The meeting request, regardless of the submission method, should include adequate information for the FDA to assess the potential utility of the meeting and to identify FDA staff necessary to discuss proposed agenda items. The meeting request should include the following information:

1. Product name.

2. Application number (if applicable).

3. Proposed proper name (or proper name if post-licensure).

[15] See http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/default.htm#Addresses.

4. Structure (if applicable).

5. Reference product name.

6. Proposed indication(s) or context of product development.

7. Meeting type being requested (i.e., Biosimilar Initial Advisory meeting, BPD Type 1, 2, 3, or 4 meeting). The rationale for requesting the meeting type should be included.

8. A brief statement of the purpose of the meeting. This statement should include a brief background of the issues underlying the agenda. It also can include a brief summary of completed or planned studies and clinical trials or data that the sponsor or applicant intends to discuss at the meeting, the general nature of the critical questions to be asked, and where the meeting fits in overall development plans. Although the statement need not provide detailed documentation of trial designs or completed studies and clinical trials, it should provide enough information to facilitate understanding of the issues, such as a small table that summarizes major results.

9. A list of the specific objectives/outcomes the requester expects from the meeting.

10. A proposed agenda, including estimated times needed for each agenda item.

11. A list of questions, grouped by discipline. Each question should be precise, and there should be a brief explanation of the context and purpose for each question.

12. A list of all individuals with their titles and affiliations who will attend the requested meeting from the sponsor's or applicant's organization and consultants.

13. A list of FDA staff, if known, or disciplines, asked to participate in the requested meeting.

14. Suggested dates and times (e.g., morning or afternoon) for the meeting that are within or beyond the appropriate time frame of the meeting type being requested.

15. The proposed format of the meeting (i.e., face-to-face meeting, teleconference, or videoconference).

The sponsor or applicant should define in its written meeting request the specific areas of input needed from CBER or CDER. A well-written meeting request that uses the above components as a guide can help the FDA understand and assess the utility and timing of the meeting related to product development or review. Although CBER or CDER will make the final determination as to the meeting type (i.e., Biosimilar Initial Advisory meeting, or BPD Type 1, 2, 3, or 4 meeting), the sponsor or applicant should provide its meeting type assessment as it relates to the product's development. The list of sponsor or applicant attendees and the list of requested FDA attendees can be useful in providing or preparing for the input needed at the meeting. However, during the time between the request and the meeting, the projected attendees can change.

Therefore, an updated list of attendees with their titles and affiliations should be provided to the appropriate FDA contact at least 1 week before the meeting.

The objectives and agenda provide overall context for the meeting topics, but it is the list of questions that is most critical to understanding the kind of information or input needed by the sponsor or applicant and to focus the discussion, should the meeting be granted. Each question should be precise and include a brief explanation of the context and purpose of the question.

VII. ASSESSING MEETING REQUESTS

The meeting request should be accompanied by the meeting package (see section X., Meeting Package Content and Submission, for additional information regarding the content of the meeting package). This ensures that the FDA will have adequate information to assess the potential utility of the meeting and prepare for the meeting. If the meeting package is not submitted to the appropriate division with the meeting request, the meeting request will be considered incomplete and the FDA generally will deny the meeting. The CBER or CDER division director or designee who receives a meeting request will determine whether to hold the meeting and will respond to the sponsor or applicant by granting or denying the meeting within 14 calendar days of receipt of the request and meeting package for a BPD Type 1 meeting, and within 21 calendar days of receipt of the request and meeting package for a Biosimilar Initial Advisory meeting or a BPD Type 2, 3, or 4 meeting.

A. Meeting Denied

If a meeting request is denied, notification to the sponsor or applicant will include an explanation of the reason for the denial. Denials will be based on a substantive reason, not merely on the absence of a minor element of the meeting request or a minor element of the meeting package. For example, as noted in section IV., Participation in the FDA's Biosimilar Biological Product Development Program, the FDA will deny a BPD Type 1, 2, 3, or 4 meeting if the sponsor or applicant is in arrears with respect to an annual BPD fee for that product.[16] Additionally, a meeting can be denied because it is premature for the product development stage or is clearly unnecessary. However, if a sponsor or applicant is not in arrears with respect to an annual BPD fee for a product, requests for BPD Type 2, 3, and 4 meetings for that product will be honored except in the most unusual circumstances.

Following denial of a meeting, a subsequent request to schedule the meeting will be considered as a new request (i.e., a request that merits a new set of time frames as described in section V., Meeting Procedures).

B. Meeting Granted

If a meeting request is granted, CBER or CDER will notify the sponsor or applicant in writing of the decision and schedule the meeting by determining the meeting type, date, time, length, place, format (i.e., a scheduled face-to-face meeting, teleconference, or videoconference), and expected

[16] See section 744H(a)(1)(E) of the FD&C Act.

FDA participants. All of the scheduling information will be forwarded to the sponsor or applicant as soon as possible following the granting notification, and within the specified BsUFA timelines.

The Center (i.e., CBER or CDER) may determine that a different meeting type is more appropriate and it may grant a meeting of a different type than requested (e.g., if a sponsor or applicant requests a Biosimilar Initial Advisory meeting for a product, but the Center determines that a BPD Type 3 meeting is more appropriate, the FDA may grant a BPD Type 3 meeting instead of a Biosimilar Initial Advisory meeting).

As described in section IV., Participation in the FDA's Biosimilar Biological Product Development Program, if the FDA grants a request for a BPD Type 1, 2, 3, or 4 meeting for a product, the sponsor or applicant may be required to pay an initial BPD fee or a reactivation fee for the product within 5 calendar days.[17]

VIII. RESCHEDULING MEETINGS

Occasionally, circumstances arise that necessitate the rescheduling of a meeting either by the FDA or the sponsor or applicant. If a meeting needs to be rescheduled, it should be rescheduled as soon as possible after the original date. A new meeting request should not be submitted and new time frames should not be set for rescheduled meetings. Sponsors or applicants and the FDA should take reasonable steps together to avoid rescheduling meetings. For example, if an attendee becomes unavailable, a substitute can be identified, or comments on the topic that the attendee would have addressed can be forwarded to the sponsor or applicant following the meeting. It will be at the discretion of the appropriate division whether the meeting should be rescheduled depending on the specific circumstances.

The following situations are examples of when a meeting can be rescheduled. This list includes representative examples and is not intended to be an exhaustive list.

- The review team determines that additional information is needed from the sponsor or applicant for the FDA to address the sponsor's or applicant's questions or other important issues for discussion, and it is possible to identify the additional information needed and arrange for its submission in a timely manner.

- Essential attendees are no longer available for the scheduled date and time because of an emergency.

- After the meeting package is submitted but before preliminary responses are sent by the FDA, the sponsor or applicant sends CBER or CDER additional questions or data that are intended for discussion at the meeting and require additional review time.

[17] See section 744H(a)(1)(A) and (D) of the FD&C Act.

- It is determined that attendance by additional FDA organizations not originally anticipated or requested by the sponsor or applicant, such as the Office of the Chief Counsel, are critical and their availability precludes holding the meeting on the original date.

IX. CANCELLING MEETINGS

When the FDA grants a request for a BPD Type 1, 2, 3, or 4 meeting for a product, the sponsor or applicant may be required to pay an initial BPD fee or a reactivation fee for the product within 5 calendar days.[18] If the sponsor or applicant fails to pay the fee within the required time frame, the meeting will be cancelled.[19] If the sponsor or applicant pays the initial BPD fee or reactivation fee after the meeting has been cancelled because of nonpayment, the time frame described in section V., Meeting Procedures, for the new meeting will be calculated from the date on which the FDA received the payment, rather than the date on which the sponsor or applicant originally submitted the meeting request.

Occasionally, other circumstances arise that necessitate the cancelling of a meeting. If a meeting is cancelled for reasons other than nonpayment of a required initial BPD fee or reactivation fee, the FDA will consider a subsequent request to schedule a meeting to be a new request (i.e., a request that merits a new set of time frames as described in sections V., Meeting Procedures, and VII., Assessing Meeting Requests). Both sponsors or applicants and the FDA should take reasonable steps to avoid cancelling meetings (unless the meeting is no longer necessary). It will be at the discretion of the appropriate division whether the meeting should be cancelled depending on the specific circumstances.

The following situations are examples of when a meeting can be cancelled. This list includes representative examples and is not intended to be an exhaustive list.

- If the FDA grants the sponsor's or applicant's meeting request, but the sponsor or applicant subsequently fails to pay a required initial BPD fee, annual BPD fee, or reactivation fee within the time frame required under section 744H(a)(1)(A), (B), or (D) of the FD&C Act, as applicable.

- The sponsor or applicant determines that the written premeeting responses to its questions are sufficient for its needs and additional discussion is not necessary (see section XII., Procedures for the Conduct of Meetings). In this case, the sponsor or applicant should contact the CBER or CDER regulatory project manager to request cancellation of the meeting. The division will consider whether it agrees that the meeting should be cancelled. Some meetings can be valuable because of the discussion they generate and the opportunity for the division to ask about relevant matters, even if the premeeting communications seem sufficient to answer the sponsor's or applicant's questions. If the division agrees with the sponsor or applicant that the meeting can be cancelled, the

[18] See section 744H(a)(1)(A) and (D) of the FD&C Act.

[19] See section 744H(a)(1(E) of the FD&C Act.

division will document the reason for cancellation and the premeeting communication will represent the final responses and the official record of the meeting.

- The FDA determines that the meeting package is grossly inadequate. Meetings are scheduled on the condition that appropriate information to support the discussion has been submitted. Adequate planning by the sponsor or applicant should avoid this problem.

X. MEETING PACKAGE CONTENT AND SUBMISSION

Premeeting preparation is critical for achieving a productive discussion or exchange of information. Preparing the meeting package should help the sponsor or applicant focus on describing its principal areas of interest. The meeting package should provide information relevant to the discussion topics and enable the FDA to prepare adequately for the meeting.

A. Timing of Submission

As discussed in section VII., Assessing Meeting Requests, if the meeting package is not submitted with the meeting request to the appropriate division, the meeting request will be considered incomplete and the FDA generally will deny the meeting.

B. Where and How Many Copies of Meeting Packages to Send

An archival copy of the meeting package should be submitted to the relevant application (e.g., IND or BLA); if there is no established application (e.g., for a pre-IND meeting), the responsible point of contact in the division will provide instructions on how to submit the meeting packages. The FDA strongly encourages sponsors or applicants to submit the archival meeting package electronically according to the electronic submission formatting recommendations (see the draft guidance for industry *Providing Regulatory Submissions in Electronic Format — General Considerations*).[20]

The number of copies of a meeting package will vary based on the meeting. The responsible point of contact in the division will advise on the number of copies needed for the meeting attendees. To facilitate the meeting process, the FDA strongly suggests that copies of meeting packages provided in electronic format also be provided in paper.

C. Meeting Package Content

The meeting package should provide information relevant to the product, development stage, and meeting type requested (see section III., Meeting Types), in addition to any supplementary information needed to develop responses to issues raised by the sponsor or applicant or division. The meeting package should contain sufficient detail to meet the intended meeting objectives. For example, inclusion of raw data rather than the derived conclusions may be appropriate in

[20] When final, this guidance will represent the FDA's current thinking on this topic.

some situations. Similarly, merely describing a result as *significant* does not provide the division with enough information to give good advice or identify important problems the sponsor or applicant may have missed. FDA guidances identify and address many issues related to biosimilar biological product development and should be considered in planning, developing, and providing information needed to support a meeting with the FDA.[21] If a product development plan deviates from current guidances, or from current practices, the deviation should be recognized and explained. Known or expected difficult design and evidence issues should be raised for discussion (e.g., selection of study populations, doses, or endpoints different from those studied for the reference product's licensure; extrapolation of indications).

To facilitate FDA review, the meeting package content should be organized according to the proposed agenda. The meeting package should be a sequentially paginated document (individual sections can be numbered separately, as long as there is an overall pagination covering the whole submission) with a table of contents, appropriate indices, appendices, cross references, and tabs differentiating sections. Meeting packages generally should include the following information:

1. Product name and application number (if applicable).

2. Proposed proper name (or proper name if post-licensure).

3. Structure (if applicable).

4. Reference product name.

5. Proposed indication(s) or context of product development.

6. Dosage form, route of administration, dosing regimen (frequency and duration), and presentation(s).

7. A list of sponsor or applicant attendees, affiliations, and titles.

8. A background section that includes the following:

    a. A brief history of the development program.

    b. The status of product development (e.g., chemistry, manufacturing, and controls; nonclinical; and clinical, including any development outside the United States, as applicable).

9. A brief statement summarizing the purpose of the meeting.

10. A proposed agenda.

[21] See the draft guidances for industry *Scientific Considerations in Demonstrating Biosimilarity to a Reference Product*, *Quality Considerations in Demonstrating Biosimilarity to a Reference Protein Product*, and *Biosimilars: Questions and Answers Regarding Implementation of the Biologics Price Competition and Innovation Act of 2009*. When final, these guidances will represent the FDA's current thinking on these topics.

11. A list of questions for discussion grouped by discipline and with a brief summary for each question to explain the need or context for the question.

12. Data to support discussion organized by discipline and question. The level of detail of the data should be appropriate to the meeting type requested and the product development stage.

XI. PREMEETINGS AND COMMUNICATIONS WITH SPONSORS OR APPLICANTS

CBER and CDER hold internal meetings, including meeting with the Biosimilar Review Committee (BRC),[22] to discuss meeting packages and to gain internal agreement on the preliminary responses to a sponsor's or applicant's questions. The FDA may communicate these preliminary responses to the sponsor or applicant. Communications before the meeting between sponsors or applicants and the FDA, including preliminary responses, can serve as a foundation for discussion or can be the final meeting responses. A preliminary response should not be construed as *final* unless there is agreement between the sponsor or applicant and the FDA that the response constitutes the FDA's final response and additional discussion is not necessary. Preliminary responses communicated by the FDA are not intended to generate the submission of a new meeting agenda and new questions. If, however, a sponsor or applicant provides new data or a revised or new proposal, the FDA may not be able to provide comments on the new data or it may generate the need for the submission of a new meeting request by the sponsor or applicant.

XII. PROCEDURES FOR THE CONDUCT OF MEETINGS

Meetings will be chaired by an FDA staff member and will begin with introductions and a statement of the agenda. Presentations by sponsors or applicants generally are not needed because the information necessary for review and discussion should be part of the meeting package. If a sponsor or applicant plans to make a presentation, the presentation should be discussed ahead of time with the CBER or CDER point of contact to determine if a presentation is warranted and to ensure that CBER or CDER has the presentation materials ahead of the meeting if possible. All presentations should be kept brief to maximize the time available for discussion.

The length of the meeting will not be increased to accommodate a presentation. If a presentation contains more than a small amount of new data that are distinct from clarifications or explanations of previous data and that were not included in the original meeting package submitted to CBER or CDER for review, FDA staff may not be able to provide comments on the new data.

[22] For more information about the BRC, refer to the Web page on implementation of the BPCI Act at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/ucm215089.htm.

Before the end of the meeting, FDA attendees and the sponsor or applicant attendees should summarize the important discussion points, agreements, clarifications, and action items. Generally, the sponsor or applicant will be asked to present the summary to ensure that there is mutual understanding of meeting outcomes and actions. FDA staff can add or further clarify any important points not covered in the summary and these items can be added to the meeting minutes. The summary can be done at the end of the meeting or after the discussion of each question.

XIII. DOCUMENTATION OF MEETINGS

Documentation of meeting outcomes, agreements and disagreements, issues for further discussion, and action items is critical to ensuring that this information is preserved for meeting attendees and future reference. FDA minutes are the official record of the meeting. The official, finalized minutes will be issued to all FDA attendees (with copies to appropriate files) and to the sponsor or applicant within 30 days of the meeting.

XIV. RESOLUTION OF DISPUTE ABOUT MINUTES

This section refers to disputes about the accuracy and sufficiency of the minutes, not to whether the positions taken by the FDA are the correct ones. The latter is subject to the standard appeal procedures (21 CFR 10.75 and 21 CFR 312.48).

A sponsor or applicant who objects to the accuracy of the minutes or who needs additional clarification of the meeting minutes issued by the FDA should contact the assigned FDA point of contact. If a sponsor or applicant needs to discuss additional issues that were not addressed at the meeting, it should submit a correspondence or a new meeting request.

If, after following up as described above, there are still significant differences in understanding regarding the content of the official meeting minutes, the sponsor or applicant should notify the FDA in writing of specific disagreements. The sponsor or applicant should submit the correspondence to its application or, if there is no application, forward a letter to the division director of the responsible division, with a copy to the point of contact describing the concerns.

The sponsor’s or applicant’s concerns will be taken under consideration by the division and the office director if the office director was present at the meeting. If the minutes are deemed an accurate reflection of the meeting discussion, the point of contact will convey this decision to the sponsor or applicant and the minutes will stand as the official documentation of the meeting. If after discussions with the sponsor or applicant the FDA deems it necessary to effect a change to the official minutes, the changes will be documented in an addendum to the official minutes. The addendum will also document any continued sponsor or applicant objections.